201-14074

HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

TEST PLAN

for

2-CYCLOHEXENE-1-OCTANOIC ACID, 5 (OR 6)-CARBOXY-4-HEXYL

CAS NO 53980-88-4

Submitted to the US EPA

by

MeadWestvaco Corporation

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Summary

MeadWestvaco Corporation is sponsoring 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl under the HPV Chemical Challenge Program. This test plan addresses the available data on this substance and proposes testing as appropriate.

This sponsored substance is a branched, C-21 dicarboxylic acid composed of saturated alkyl chains and a cyclohexene branch. The substance is supplied commercially as Westvaco DIACID® 1550. This is a class 2 product containing several components, being a mixture of about 60-70% of the C-21 diacid, 20-25% unreacted C-18 monoacid and 5-10% C-36 dimer acid.

In general, testing has and will be carried out using Westvaco DIACID® 1550. In some cases it is desirable to maximize the concentration of test substance dissolved in water and so the potassium salt has been used, as the commercial product Westvaco DIACID® H-240.

Westvaco DIACID® 1550 is manufactured by a patented process from tall oil fatty acids, which are obtained by the fractional distillation of crude tall oil, a by-product from the pulping of pine trees. Tall oil fatty acids and some other similar substances have been sponsored under the HPV chemical challenge program by the Pine Chemicals Association HPV task force (PCA), of which MeadWestvaco Corporation is a member.

Although there are some similarities between 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and the chemicals sponsored by the PCA, there are also differences. Hence, data on tall oil fatty acids and other substances cannot be read across to meet SIDS endpoints for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. However, these data have been used as supporting information to gain a broader view of the properties of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl in cases where testing has not been performed, and also in assessing requirements for further testing.

Physicochemical properties

The **melting point** will not be determined because the substance is a liquid. Also, as a class 2 substance, it is unlikely to give a sharp freezing point.

The **boiling point** cannot be determined because the substance will decompose, possibly explosively, before it boils.

The **vapor pressure** is negligible under ambient conditions and will not be determined.

Adequate data are available for the **partition coefficient**.

The **water solubility** will be determined.

Environmental Fate

Adequate **biodegradation** data are available.

Hydrolysis will not be determined because the substance has a very low solubility in water and lacks a functional group that would be susceptible to hydrolysis.

Determination of **photodegradation** is not relevant since the vapor pressure of the substance is essentially zero and it will not enter the atmosphere.

Transport and distribution between environmental compartments will not be determined due to the inability to provide usable inputs for the required modelling.

Ecotoxicity

The potassium salt has been used in tests to determine the **acute toxicity to fish, daphnia and algae**. Adequate data are available and no further testing is necessary.

Human health Effects (Mammalian) Toxicity

Adequate data are available for **bacterial and non-bacterial genotoxicity** and **acute oral toxicity**. No data are available for **subchronic toxicity**, **toxicity to reproduction** and **developmental toxicity** and testing following the OECD 422 combined test guideline will be undertaken to address these SIDS endpoints.

I Description of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl

A 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl

The compound 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl (CAS Registry Number 53980-88-4) is being sponsored by MeadWestvaco Corporation under the US EPA HPV chemical challenge program. This substance is a branched, C-21 dicarboxylic acid composed of saturated alkyl chains and a cyclohexene branch. The substance is supplied commercially as Westvaco DIACID® 1550. This is a class 2 product containing several components, being a mixture of about 60-70% of the C-21 diacid, 20-25% unreacted C-18 monoacid and 5-10% C-36 dimer acid.

Westvaco DIACID® 1550 is manufactured by a patented process from tall oil fatty acids, which are obtained by the fractional distillation of crude tall oil, a by-product from the pulping of pine trees. Westvaco DIACID® 1550 is used as a surfactant in a wide range of applications. It also provides lubrication and corrosion protection in metalworking applications and acts as an hydrotrope for nonionic surfactants in alkaline cleaner formulations.

B Related Compounds

There are several related materials that should be considered, as data on the properties of these substances may potentially be read across to meet data requirements for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. These related substances have been sponsored under the HPV chemical challenge program by the Pine Chemicals Association HPV task force (PCA), of which MeadWestvaco Corporation is a member.

The first set of related compounds are six substances forming the “Tall Oil Fatty Acids and Related Substances” group. Tall oil fatty acids (CAS Registry Number 61790-12-3) are of obvious relevance since they are the precursor of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and are present in the Westvaco DIACID® 1550 product. Tall oil fatty acids are also the dominant member of the “Tall Oil Fatty Acids and Related Substances” group, being the substance with by far the greatest production volume of the substances in this group. Tall oil fatty acids typically contain a combined total of about 80% of oleic and linoleic acids. These are unsubstituted, linear, C-18, mono- or di- unsaturated monocarboxylic acids.

Also of some relevance in the “Tall Oil Fatty Acids and Related Substances” group are fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear (CAS Registry Number 68955-98-6), also known as monomer acid. This substance is a complex mixture. It typically contains about 36% oleic and elaidic acids, which are *cis* and *trans* forms of unsubstituted, linear C-18 monounsaturated monocarboxylic acids. Fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear also typically contain 28% of other branched C-18 acids and 24% of other C-18 acids, probably cyclic acids of unknown structure. Fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear have

similarities to tall oil fatty acids but contain a much lower level of unsaturation and also contain some branched and cyclic chains. Because of this, fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear share some characteristics with 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. There are however differences in the numbers of carbon atoms and carboxylic acid groups in the molecules.

The original test plan for the "Tall Oil Fatty Acids and Related Substances" group was posted on the HPV web site on 14th June 2001 and the PCA responded to all comments with a revised test plan on 5th March 2002.

This revised test plan for the "Tall Oil Fatty Acids and Related Substances" group will provide data on the water solubility, partition coefficient and biodegradability of all six members. However, toxicological testing will only be carried out on tall oil fatty acids and fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear. The toxicological properties of the other group members will be read across from these substances.

The other group of chemicals sponsored by the PCA that is of interest is the "Fatty Acid Dimers and Trimer" group. The dimer is manufactured from C-18 unsaturated fatty acids and consists of many geometric isomers of C-36 dicarboxylic acids with a low level of unsaturation. The compounds may be acyclic, cyclic, aromatic or polycyclic. Apart from the presence of C-36 dimer in Westvaco DIACID® 1550, the relevance of dimer is that it is also composed of branched dicarboxylic acids, although they have a much higher molecular weight than 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and a wide range of isomeric structures.

The proposed test plan for this category was posted on the HPV web site on 4th April 2002, and following the receipt of comments, a revised test plan was posted on the EPA HPV web site on 10th November 2002. Dimer is the primary substance in this group, which has three other members. It is proposed that water solubility, partition coefficient and biodegradation data will be developed for these other three members but that toxicological data will be read across from that for dimer.

C Use of Data on Related Compounds

Taken together, these related substances (tall oil fatty acids, dimer and fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear) share some characteristics with 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. They are all long chain alkyl carboxylic acids with various degrees of branching and unsaturation. The major feature that distinguishes 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl from all the related compounds is that it is a C-21 compound. Also, it is a diacid, a feature shared only with the dimer molecule.

Hence any proposed read across of data from these other substances to 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl needs to be supported by evidence of comparability. This additional information must show that other, relevant, properties of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl are similar to those of the compounds from which data are being read across. This is an important consideration since the PCA, following comments from the EPA, decided not to read across data from

tall oil fatty acids to fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear, even although these substances are within a single chemical category.

In view of these concerns regarding the read across of data and the differences and similarities between the molecules, it is considered that it is not possible to read data directly across from these related substances to 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. However, the test plan for to 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl bears many similarities to the test plans for the related substances, reflecting the common features of all four substances.

D Choice of Test Substance

The sponsored chemical, 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl is not supplied and used as an isolated molecule but as the major constituent of a commercial product, Westvaco DIACID® 1550. Therefore, testing, in general, will be carried out using Westvaco DIACID® 1550 as the test substance as this is the substance used commercially.

However, 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and Westvaco DIACID® 1550 have only low solubilities in water. For the evaluation of some properties, the test substance used was Westvaco DIACID® H-240. This is a 40% solution of the potassium salt of Westvaco DIACID® 1550 and maximizes the solubility of the test substance. A similar approach to provide greater solubility of the test substance has been adopted by the PCA in the revised test plan for the “Tall Oil Fatty Acids and Related Substances” group, with fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear being tested as the sodium salt.

II Review of Existing data and Development of Test Plan

A Overview

The data available on the SIDS endpoints of concern for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl have been subject to a comprehensive review. Both the current state of knowledge and the reliability of the data have been assessed, together with corresponding data and test plans for the related compounds. A test plan has subsequently been drawn up so that all relevant SIDS endpoints may be addressed satisfactorily to meet the commitment of MeadWestvaco Corporation in sponsoring 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl under the EPA HPV Chemical Challenge Program.

The availability of data for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl (as Westvaco DIACID® 1550) is shown in Table 1. This table also shows data gaps that will be addressed by additional testing and the corresponding plans from the PCA for tall oil

fatty acids, dimer and fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear.

Table 1
Matrix of Available Adequate data and Future Testing on 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl and Related Substances.

SIDS endpoint	Westvaco DIACID® 1550	Tall Oil Fatty Acids (revised plan)	Monomer Acid (b) (revised plan)	Dimer (revised plan)
melting point	do not test	do not test	do not test	do not test
boiling point	do not test	do not test	do not test	do not test
vapor pressure	do not test	do not test	do not test	do not test
water solubility	test	test	test	test
partition coefficient	available	test	available	test
biodegradation	available (a)	available	test	available
hydrolysis	do not test	do not test	do not test	do not test
photodegradation	do not test	do not test	do not test	do not test
transport / distribution	do not test	do not test	do not test	do not test
toxicity to fish	available (a)	test	test	test
toxicity to *Daphnia*	available (a)	test	test	test
toxicity to algae	available (a)	test	test	test
acute toxicity	available	available	test	available
subchronic toxicity	test (c)	available	test	available
mutagenicity – bacterial	available	available	test	available
mutagenicity – mammalian	available	available	test	available
toxicity to reproduction	test (c)	available	test	test
developmental toxicity	test (c)	available	test	test

(a) – test carried out on potassium salt, Westvaco DIACID® H-240
(b) – "monomer acid" is alternative name for "fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear"
(c) – combined test following OECD guideline 422

As may be seen, the test plan will result in data availability for 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl identical to that of the related substances (tall oil fatty acids, dimer and fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear) in the two test groups sponsored by the PCA.

B Evaluation of Physicochemical Data and Required Testing

The basic physicochemical data required in the SIDS battery are melting point, boiling point, vapor pressure, partition coefficient and water solubility.

Class 2 substances are composed of a complex mixture of molecules that are often difficult to characterize. Westvaco DIACID® 1550 is derived from natural sources of variable composition that cannot be represented by a definite chemical structure. Due to this complex composition some measurements of physical properties are likely to produce results that are erroneous, difficult to interpret or meaningless.

In principle, testing of physicochemical properties could be carried out on 2-cyclohexene-1-octanoic acid, 5-carboxy-4-hexyl or 2-cyclohexene-1-octanoic acid, 6-carboxy-4-hexyl, if these compounds were isolated from the Westvaco DIACID® 1550 product. However, such information would be of little practical use in evaluating the properties of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl under the HPV Chemical Challenge Program. Isolation and testing using 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl will therefore not be carried out within the test programme.

B1 Melting Point

Westvaco DIACID® 1550 is a liquid under normal conditions and determination of the melting point is not applicable. While consideration can be given to measurement of a freezing point, this is not likely to provide any useful information since Westvaco DIACID® 1550 is a complex mixture. It is therefore likely not to provide a defined freezing point but to display freezing behavior over a range of temperatures. Therefore, determination of the melting point will not be attempted.

B2 Boiling Point

Westvaco DIACID® 1550 is a non-volatile liquid at ambient temperatures and will decompose if heated to high temperatures. According to the material safety data sheet, the boiling point is in excess of 260ºC, while the flash point is 235ºC. Explosive mixtures may be formed at temperatures at, above, or, in some circumstances, below the flash point. Hence the boiling point will not be determined as such measurements serve no value within the HPV Chemical Challenge Program, while performing the required experiment would be potentially dangerous.

B3 Vapor Pressure

The vapor pressure of Westvaco DIACID® 1550 at ambient temperatures is effectively zero, and experimental measurement is inappropriate.

B4 Water Solubility

The solubility in water of Westvaco DIACID® 1550 will be determined following OECD guideline 105.

B5 Octanol – Water Partition Coefficient

Testing has been recently been performed to generate adequate data showing that the log K_{ow} for Westvaco DIACID® 1550 at pH 2 is approximately 7.09, this being the mean of two peaks observed under the experimental conditions. No further testing to ascertain the

partition coefficient will be undertaken, although the report notes that the values obtained are outside the specified range (0 to 6) for the method used. Multiple values for the partition coefficient would be expected since the substance is a mixture of several compounds.

Summary of Physicochemical Properties Testing: The water solubility will be determined. Adequate data are available for the partition coefficient. Tests for melting point, boiling point and vapor pressure are inappropriate.

C Evaluation of Environmental data and Required Testing

The fate and behavior of a chemical in the environment is determined by the rates of the most important transformation (degradation) processes. The basic environmental fate data covered by the HPV Chemical Challenge Program include biodegradation, stability in water (hydrolysis as a function of pH), photodegradation and transport and distribution between environmental compartments.

C1 Biodegradation

Data and robust study summaries are available. Because of the low solubility in water of Westvaco DIACID® 1550, the tests were carried out using the potassium salt, Westvaco DIACID® H-240. When tested for ready aerobic biodegradability following OECD guideline 301E the material was found not to be readily biodegradable, showing 63% degradation after 35 days. However, when tested for biodegradation using anaerobic sludge as specified in EPA OTS method 40 CFR 796.3140 (now EPA OPPTS harmonized guideline 835.3400), biodegradation of up to 84% was observed within 56 days. This method is used for screening for the anaerobic biodegradability of organic compounds. A high biodegradability result in this test provides evidence that the test substance will be biodegradable in sewage treatment plant anaerobic digestors and in many natural anaerobic environments such as swamps, flooded soils, and surface water sediments.

Westvaco DIACID® H-240 contains not only the potassium salts of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl but also the salts of the unreacted C-18 monoacid and C-36 dimer acid. Information on the biodegradability of the C-18 monoacid and its potassium salt and C-36 dimer acid has been previously submitted by the PCA under the HPV Chemical Challenge Program. The available information shows that the C-18 monoacid and its salt typically demonstrate 55 to 85% biodegradability over 28 days whereas the dimer acid demonstrated only around 6.5 % biodegradability over the same period. While the various results cannot be directly compared because of the differences in test methods and conditions, it nevertheless appears that the biodegradability of Westvaco DIACID® H-240 is similar to that of the C-18 monoacid and much greater than that of the C-36 dimer acid. This suggests that although 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl may not meet the criterion of being readily biodegradable, it nevertheless would exhibit a significant degree of biodegradability if tested.

On this basis, the available data are considered adequate and no further testing will be carried out.

C2 Hydrolysis

Hydrolysis as a function of pH is a measure of the stability of a substance in water. Westvaco DIACID® 1550 does not contain any organic functional groups susceptible to hydrolysis. In addition, low solubility in water often limits the ability to determine hydrolysis and Westvaco DIACID® 1550 has a very low solubility in water. Therefore, this test material is expected to be stable in water and testing of hydrolytic stability as a function of pH is not considered applicable.

C3 Photodegradation

No information is available on the photodegradation of Westvaco DIACID® 1550. However, since the substance is not volatile, it will not enter the atmosphere and be subject to photodegradation. Additionally, the chemical structures suggest that the molecules would not be susceptible to breakdown by a photodegradative mechanism. For these reasons, testing for photodegradation is not considered applicable.

C4 Transport and Distribution

Transport and distribution between environmental compartments is intended to determine the ability of a chemical to move and partition in the environment. Such information is generated from models such as the level III model from the Canadian Environment Modelling Centre at Trent University. Use of these models requires the input of a range of parameters. For class 2 substances the required inputs are often not available or impossible to determine. Use of the model would not only require the input of multiple parameters but also potentially present multiple outputs for individual constituents of the product. These would not form a reasonable representation of the environmental distribution of the product. For these reasons, even although no information is available on the environmental transport and distribution of Westvaco DIACID® 1550, no work to assess the environmental transport and distribution of this substance will be performed.

Summary of Environmental Fate Testing: Biodegradation data are available. Determinations of photodegradation, hydrolysis and transport and distribution between environmental compartments are inapplicable.

D Evaluation of Ecotoxicity Data and Required Testing

The basic ecotoxicity data that are part of the HPV Chemical Challenge Program are acute toxicity to fish, daphnia and algae. Because of the low solubility in water of Westvaco DIACID® 1550, these tests were carried out using the potassium salt, Westvaco DIACID® H-240. This maximizes the concentration of test material to which the test organisms can be exposed while minimizing the potential for physical toxicity arising from the formation of features such as dispersions or critical micelles.

D1 Acute Toxicity to Fish

Testing has been performed and a robust test summary is available. The 96 hour LC_{50} to the fresh water minnow, *Pimephales promelas*, was found to be 15 mg/l. The No Observed Effect Concentration was 9.8 mg/l. No further testing is required.

D2 Acute Toxicity to Daphnia

Testing has been performed and a robust test summary is available. The 48 hour LC_{50} to the water flea, *Daphnia pulex*, was found to be 22.5 mg/l. The No Observed Effect Concentration was 9.8 mg/l. No further testing is necessary.

EPA guidance (*Federal Register,* Vol 65 No 248 page 81695) recommends that, for chemicals with a log K_{ow} value greater than 4.2, a test of chronic toxicity to *Daphnia* is carried out rather than tests of the acute toxicity of the material to *Daphnia* and fish. This is due to concerns about the potential for bioaccumulation of such test materials. However, the very high partition coefficient and the very low water solubility of Westvaco DIACID® 1550 together indicate that bioaccumulation is unlikely. Since data from acute tests are already available, it is considered that a 21-day test with *Daphnia* would produce no additional data of benefit, although considerable practical difficulties could arise in attempting to perform such a test.

D3 Acute Toxicity to algae

Testing has been performed and a robust test summary is available. The 96 hour EC_{50} to S*elenastrum capricornutum* was found to be 87.6 mg/l. The approximate No Observed Effect Concentration was 32 mg/l. No further testing will be performed.

Summary of Ecotoxicity Testing: The acute toxicity of Westvaco DIACID® H-240 (the potassium salt of DIACID® 1550) to fish, daphnia and algae has been determined. Adequate data are available and no further testing is necessary.

E Evaluation of Human Health Effects and Required Testing

The basic toxicity data required under the HPV Chemical Challenge Program are acute and repeated dose toxicity, bacterial and non-bacterial genotoxicity and developmental and reproductive toxicity.

E1 Acute Oral Toxicity

Testing has been performed with Westvaco DIACID® 1550 and a robust test summary is available. The LD_{50} to Sprague-Dawley rats, following a non-standard protocol, was found to be 6176 mg/kg bw. This study has a Klimish Reliability code of 2 – reliable with restrictions.

In other testing reported by the PCA, the acute oral toxicity of dimer, in three tests following the OECD 401 protocol, has been found be >5000 mg/kg bw for Wistar rats and >2000 mg/kg bw for Sprague-Dawley rats. The acute oral toxicity of tall oil fatty acids, also following the OECD 401 protocol, was >10000 mg/kg bw. The revised test plan from the PCA for the "Tall Oil Fatty Acids and Related Substances" group also includes determination of the acute oral toxicity of the sodium salt of fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear.

Although existing data on the acute oral toxicity of Westvaco DIACID® 1550 were generated using a non-standard protocol, all currently available test results indicate that these long chain fatty acids have low acute oral toxicity. Therefore, no further testing of Westvaco DIACID® 1550 will be performed.

E2 Subchronic Toxicity

No information is available on the subchronic toxicity of Westvaco DIACID® 1550. The PCA has reported that tall oil fatty acids have been tested for repeat dose toxicity in a 90 day study and found to have low toxicity, with a no observed effect level (NOEL) of approximately 2500 mg/kg bw/day. Dimer has been similarly tested and also found to be of low toxicity. Although a NOEL was not established, the tests revealed a no observed adverse effect level (NOAEL) of approximately 100 mg/kg bw/day. The revised test plan for the "Tall Oil Fatty Acids and Related Substances" group also includes determination of the subchronic toxicity of the sodium salt of fatty acids, C-16 to C-18 and C-18 unsaturated, branched and linear.

The need to establish the subchronic toxicity of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl has been carefully considered. All available data for acute and subchronic toxicity of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl, tall oil fatty acids and dimer indicate low toxicities. This leads to the expectation that 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl also has a low subchronic toxicity. This could result in an opinion that further testing, which would require the use of vertebrate animals, is not justified. However, subchronic toxicity is a basic data requirement within the HPV Chemical Challenge Program. The absence of data for this end-point, together with the limited reliability of the available acute toxicity data supports the much stronger case for determining the subchronic toxicity of Westvaco DIACID® 1550. This test is typically carried out following OECD guideline 408. However, for reasons described below in sections E5 and E6, a combined subchronic toxicity and reproductive / developmental toxicity screen test (OECD 422) of Westvaco DIACID® 1550 will be performed.

E3 Bacterial Genotoxicity

Testing has been performed on Westvaco DIACID® 1550 and a robust test summary is available. The results show no evidence of mutagenicity against a range of bacteria in either the presence or absence of metabolic activation when tested at the limits of solubility and cytotoxicity.

The available data are considered adequate and no further testing is necessary.

E4 Non-bacterial Genotoxicity

Testing has been performed on Westvaco DIACID® 1550 and a robust test summary is available. The results show no significant increase in chromosomal aberrations in cultured Chinese hamster ovary cells in either the absence or presence of metabolic activation.

The available data are considered adequate and no further testing is required.

E5 Toxicity to Reproduction

No information is available on the toxicity to reproduction of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. The PCA has reported that tall oil fatty acids have been tested for reproductive toxicity in a procedure consistent with OECD method 415. Tall oil fatty acids have no effect upon reproductive capabilities at doses of approximately 5000 mg/kg bw/day. The PCA has also reported that the test for the subchronic toxicity of dimer included histopathology of the reproductive organs and showed no evidence of toxicity to these organs at any dose level.

It is therefore considered that 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl is unlikely to be toxic to reproduction. However, no data are available. Since other data gaps have been identified, as described in sections E2 and E6, a combined subchronic toxicity and reproductive / developmental toxicity screen test (OECD 422) of Westvaco DIACID® 1550 is recommended.

E6 Developmental Toxicity

No information is available on the developmental toxicity of of 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl. The PCA has reported that tall oil fatty acids have been tested for developmental toxicity in a procedure consistent with OECD method 415. Tall oil fatty acids have no effect upon developmental capabilities at doses of approximately 5000 mg/kg bw/day.

It is therefore considered that 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl is unlikely to exhibit developmental toxicity. However, no data are available. Since other data gaps have been identified, as described in sections E2 and E5, a combined subchronic toxicity and reproductive / developmental toxicity screen test (OECD 422) of Westvaco DIACID® 1550 is recommended. The adoption of this combined test guideline to address the SIDS endpoints for subchronic toxicity, toxicity to reproduction and developmental toxicity is in accordance with EPA guidance (*Federal Register,* Vol 65 No 248 page 81695).

Summary of Human Health Effects (Mammalian Toxicity) Testing: Adequate data are available for bacterial and non-bacterial genotoxicity and acute oral toxicity. No data are available for subchronic toxicity, toxicity to reproduction and developmental toxicity, although data from the PCA on similar compounds suggest that 2-cyclohexene-1-octanoic acid, 5 (or 6)-carboxy-4-hexyl will have low subchronic toxicity and no developmental or reproductive toxicity. Testing of Westvaco DIACID® 1550 following the OECD 422 guideline will take place to address these SIDS endpoints.